UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,015	10/11/2005	Nobuhiro Umeda	20241/0203472-US0	7127

7278 7590 03/30/2009

DARBY & DARBY P.C.
P.O. BOX 770
Church Street Station
New York, NY 10008-0770

EXAMINER	
OH, TAYLOR V	

ART UNIT	PAPER NUMBER
1625	

MAIL DATE	DELIVERY MODE
03/30/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/552,015	UMEDA ET AL.	
	Examiner	Art Unit	
	Taylor Victor Oh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *4-8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The Status of Claims:

Claims 1-8 are pending.

Claims 1-3 are rejected.

Claims 4-8 are withdrawn form consideration.

DETAILED ACTION

1. Claims 1-3 are under consideration in this Office Action.

Priority

2. It is noted that this application is a 371 of PCT/JP04/05240 (04/13/2004), which has foreign priority documents, Japan 2003-109665 (04/14/2003) and Japan 2004-022719 (01/30/2004).

Drawings

3. None.

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-3) on 12/18/08 is acknowledged.

Claims 4-8 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group II, there being no allowable generic or linking claim.

Applicants argue the following issue:

> 1. The unity of invention may nevertheless exist if one of the claim Groups is directed to a product and a process specially adapted for the manufacture of the said product, and the other claim group is directed to a use of the said product(37 CFR 1.475(b)(3)).

With respect to applicants' arguments, Group I and Groups II lack a special technical feature between them. In the instant case, the invention of Group II is directed to the method for treating cerebrovascular or cerebral infraction or circulatory disorder or retinal oxidation disorder or inhibiting lipoxygenase by using the following compound formula (1), whereas the invention I is related to the compound formula (1) and its pharmaceutical composition and its preparation.

The prior art Sakanaka et al (US 6,579,853) discloses the brain cell or nerve cell protective agents comprising ginsenoside RB1 useful for treating cerebrovascular or cerebral infraction or circulatory disorder or retinal oxidation disorder structurally unrelated to the claimed compounds of formula (1). Therefore, there is no special technical feature of Group I required in Group II because the ginsenoside RB1 compound in Sakanaka et al (US 6,579,853) completely different from the claimed compound can serve the same function or use as the claimed invention. There is no single general inventive concept and no unity of invention for the method or the processes as defined in 37 CFR 1.475.

Also, the two separate Groups I and II can pose undue burden on the Examiner because it requires new search due to being two different fields of inventions.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

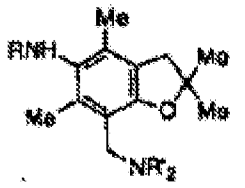
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

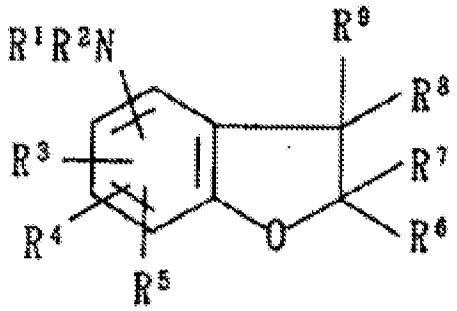
Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ohkawa et al (J. Med. Chem. 1997,40, 559-573) in view of Aono et al (EP 0483772 A1).

Ohkawa et al discloses dual inhibitors of lipid peroxidation and dopamine release with protective effects against central nervous system trauma and ischemia by using one of the aminocoumarans as shown below(see page 561, scheme 3):



19a, 19b, R = H

The instant invention, however, differs from the prior art in that the claimed RNH is an ortho-position to CH_2NME_2 with respect to the orientation on the ring instead of a meta position in the prior art.



(I)

wherein R^1 and R^2 are the same or different and are a hydrogen atom, an acyl group, an alkoxycarbonyl group, an optionally substituted aliphatic or an optionally substituted aromatic group; R^3, R^4 and R^5 are the same or different and are an optionally acylated hydroxyl group, an optionally substituted amino group, an optionally substituted alkoxy group or an optionally substituted aliphatic group, or two of R^3, R^4 and R^5 may linked together to form an optionally substituted carbocyclic group; R^6 and R^7 are the same or different and are an optionally substituted aliphatic group, provided that at least one of R^6 and R^7 has methylene at the α-position; and R^8 and R^9 are the same or different and are a hydrogen atom or an optionally substituted aliphatic group or an optionally substituted aromatic group, or a salt thereof. Further, it has been found that the novel compounds have activities useful for medicines, for example, strong lipoperoxide formation inhibitory activity and the like. Thus, the present invention has been completed.

That is, the present invention provides the novel aminocoumaran derivatives of the general formula (I) or salts thereof and a pharmaceutical composition comprising them as an active component.

(see page 2 ,lines 35-55).

Accordingly, the compound (I) of the present invention has therapeutic and preventive effects on various diseases of mammal (e.g., mouse, rat, rabbit, dog, monkey, human, etc.) such as thrombosis due to platelet aggregation; ischemic diseases due to constriction of arterial vascular smooth muscle or vasospasm in the heart, lung, brain and kidney (e.g., cardiac infarction, cerebral apoplexy, etc.); neuropathy (e.g., Parkinson's disease, Arzheimer's disease, Lou-Gehring's disease, muscular dystrophy, etc.); functional disorders caused by central damage such as cranial injury, spinal injury, etc.; dysmnesia or emotional disturbance (disorders accompanied by nerve cell necrosis caused by hypoxia, cerebral lesion, cerebral hemorrhage, cerebral infarction, cerebral thrombosis, etc.); convulsion and epilepsia caused after cerebral apoplexy, cerebral infarction, cerebral surgery or cranial injury; nephritis; pulmonary insufficiency; bronchical asthma; inflammation; arterial sclerosis; atherosclerosis; hepatitis; acute hepatitis; cirrhosis; hypersensitivity pneumonitis; immune deficiency syndrome; circulatory diseases caused by injury of enzymes, tissue, cells, etc. of the living body due to active oxygen species (e.g., superoxide, hydroxide radical, etc.) (e.g., cardiac infarction, cerebral apoplexy, cerebral edema, nephritis, etc.); tissue fibroplastic phenomenon; carcinogenesis and the like. For example, the compound (I) of the present invention is useful as medicines such as an antithrombotic drug, an antivasoconstriction drug, an antiasthmatic drug, an antiallergic drug, a drug for improving circulatory system such as the heart and brain, a drug for treating nephritis, a drug for treating hepatitis, a drug for inhibiting tissue fibroplastic, a drug for scavenging active oxygen species, a drug for regulating and improving arachidonate cascade substances and the like.

(see page 7 ,lines 12-30).

With respect to the orientation on the ring, It is well established that position isomers are prima facie structurally obvious even in the absence of a teaching to modify. The isomer is expected to be preparable by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing the position isomers. This circumstance has arisen many times. See: *Ex parte Englehardt,*

208 USPQ 343, 349; *In re Mehta,* 146 USPQ 284, 287; *In re Surrey,* 138 USPQ 67; *Ex Parte Ullyot,* 103 USPQ 185; *In re Norris,* 84 USPQ 459; *Ex Parte Naito,* 168 USPQ 437, 439; *Ex parte Allais,* 152 USPQ 66; *In re Wilder,* 166 USPQ 545, 548; *Ex parte Henkel,* 130 USPQ 474; *Ex parte Biel,* 124 USPQ 109; *In re Petrzilka,* 165 USPQ 327; *In re Crownse,* 150 USPQ 554; *In re Fouche,* 169 USPQ 431; *Ex parte Ruddy,* 121 USPQ 427; *In re Wiechert,* 152 USPQ 249, *In re Shetty*, 195 USPQ 753.

For example, "Position isomerism has been used as a tool to obtain new and useful drugs" (Englehardt) and "Position isomerism is a fact of close structural similarity" (Mehta, emphasis in the original). See also MPEP 2144.09, second paragraph.

Ohkawa et al expressly discloses dual inhibitors of lipid peroxidation and dopamine release with protective effects against central nervous system trauma and ischemia by using one of the aminocoumarans, whereas Aono et al discloses aminocoumaran derivative useful as medicines for treating various diseases such as arterial sclerosis, cerebrovascular diseases (see page 4, lines 1-6).

Both aminocoumarans compounds in the prior art have shared the common features of the claimed compounds with the same or similar utilities; therefore, if the skilled artisan in the art had desired to expand the perimeter of the treatment using aminocoumarans, it would have been obvious to the skilled artisan in the art to be motivated to combine the teaching of treating various diseases shown in the Aono et al with Ohkawa's et al method . This is because both aminocoumarans compounds in the prior art have shared the common features of the claimed compounds with the same or similar utilities; the skilled artisan in the art would expect such a manipulation to be successful and feasible as guidance shown in the prior art.

Applicants' Argument

Regarding the responses to applicants' arguments along the Declaration under 37 CFR 1.132 filed on 9/02/2008, the examiner will defer those responses until the next communication of writing up the Office Action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taylor Victor Oh whose telephone number is 571-272-0689. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Taylor Victor Oh, MSD,LAC
Primary Examiner
Art Unit :1625

/Taylor Victor Oh/
Primary Examiner, Art Unit 1625
3/24/09